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EXAMINER	
SINGH, SATYENDRA K	
ART UNIT	**PAPER NUMBER**
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,436	LYLES, MARK B.	
	Examiner	Art Unit	
	SATYENDRA K. SINGH	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,19 and 20* is/are pending in the application.

4a) Of the above claim(s) *1-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 6th 2008 has been entered.

Claims 1-10 (non-elected invention of group I) remain withdrawn from further consideration.

Claims 16-18 are canceled by applicant's amendments to claims.

Claims 11-15, 19 and 20 (group II, as currently amended) are examined on their merits in this office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 11-15, 19 and 20 (as currently amended) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 (as currently amended) recites "forming a suspension consisting of **a subject's autologous stem cells** and a soluble medium", which is confusing. It is unclear as to what exactly is encompassed by the method step as recited in the claim. It is unclear as to how,

from which tissue source, and how much of said "autologous stem cells" are obtained from the subject in order to be suspended with a soluble medium, as required by the limitation as claimed. It is also not clear if said limitation of "subject's autologous stem cells" actually refers to a purified stem cell preparation obtained from said subject, without any other type of cells contained within it, or it refers to an isolated autologous stem cell preparation that also contains other types of cells that are not stem cells.

In addition, claim 11 recites (in lines 7-8 of the instant claim, as amended) the step of "dispersing **the suspension** .....using the air-jet sprayer", which is confusing because, it is not clear if "the suspension" used in said step is dispersed through the nozzle orifice of the air-jet sprayer that has been filled with the suspension formed in the step of "forming a suspension….medium", or this method step is performed without the use of air-jet sprayer, directly using the suspension formed in the first step of the method as claimed. Appropriate explanation/correction is required.

Since, claims 12-15, 19 and 20 depend from the broader claim 11, they are also rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Response to Applicant's Arguments

Applicants argue the following (see response page 5):

> "Claims 11-17, 19, and 20 were rejected by the Examiner under 35 U.S.C. §112, second paragraph, as being indefinite and failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants amend Claims 11 and 19 to overcome these rejections and respectfully request full allowance of Claims 11-15; 19 and 20 as amended."

In response, it is noted that the instant claim 11, as currently amended, is still indefinite for the reasons discussed as above. Moreover, it is noted that applicants did not point out the support for the current amendments to the claims (i.e. claims 11 and 19, in particular), which applicants are requested to provide with any claim amendments made during future prosecution for claim amendments to be in compliance.

Claim Rejections - 35 USC § 112

The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11 (as currently amended) is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains **subject matter which was not described** in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 11 recites the newly added limitation of "**forming a suspension consisting of a subject's autologous stem cells** and a soluble medium", for which there is no support or description in the instant disclosure, original claims, drawing, or the examples provided by applicants (see instant disclosure, pages 12-24, examples 1-5, in particular). The disclosure provided by applicants in the original claims (for example, claim 11 and 18 as originally presented), while providing the basis for a method of dispersing living cells comprising the step of suspending autologous cells that may further include stem cells, does not provide an explicit support (or exemplification

or similar disclosure) for the step of "forming a suspension **consisting of** a subject's autologous stem cells and a soluble medium", as currently presented by applicants. In addition, applicant's remarks (filed with the office on March 6th 2008; see page 5, 1st paragraph, in particular) do not clearly point to an appropriate support for such a method step as recited in the instant claim 11.

Since, the claimed invention is not fully supported by the disclosure either in the narrative or generic or in the examples or in the original claims provided by applicants, the claimed limitation constitutes **a new matter situation**. Appropriate explanation/correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 11-15, 19 and 20 (as currently amended) are rejected under 35 U.S.C. 103(a) as being unpatentable over MARSHALL et al (US 6,479,052 B1; [A]) or COHEN et al (2000; [U]) and SORRELL et al (US 6,497,875 B1; [A2]).

Claims 11-15, 19 and 20 are generally directed to **a method of dispersing living cells** comprising: **forming a suspension consisting of a subject's autologous stem cells** and a soluble medium; placing the suspension into a receptacle of an air-jet sprayer (having a nozzle orifice with a pore size sufficient to allow passage of the suspension without damage); and dispersing the suspension onto an area of skin of the subject lacking normal, healthy skin using the air-jet sprayer (see detailed recitations of instant claims 14-15 and 20).

Marshall et al [A] disclose a method of dispersing autologous living cells on a skin wound (for example, keratinocytes, fibroblasts, etc.; see abstract, summary of the invention, column 2, 2nd paragraph; column 4, last paragraph, and claims, in particular) comprising suspending autologous cells in a soluble medium (see example 3, columns 12-13, in particular); placing the cells into a receptacle of **an air-jet sprayer** (having a nozzle orifice with a pore size sufficient to allow passage of cells without damage; see column 7-8); and dispersing the cells onto an area of skin of a subject (experimental animal such as Large White pig; see column 3, 1st paragraph, and example 3, in particular) lacking normal, healthy skin using the air-jet sprayer; wherein the **keratinocytes** (i.e. contained in **a cell suspension** having growth factors such as serum) are sprayed (with or without fibrin sealant, i.e. an adhesion factor) onto **a dermal graft** (such as Integra; example 3, column 13, in particular) or onto a tissue scaffold (such as fibrin matrix, or other types of biodegradable polymers; see columns 6-7, in particular). Furthermore, it is to be noted that Marshall et al [A] clearly suggest and disclose a method of dispersing living cells, wherein various types of autologous cells (including keratinocytes, fibroblasts, etc.) can be delivered **separately** onto a target

(see column 3, 1st paragraph, and column 8, 1st and 2nd paragraphs, in particular), **or in combination** (i.e. co-dispersed or co-delivered) with other autologous cells, growth factors, bioactive agents, etc. (see column 6, lines 41-46, in particular).

Cohen et al [U] teach a method of dispersing living skin epidermal cells (in a suspension wherein the cells are isolated from the skin of groin area; see abstract, and page 1210, *Materials and Methods*, in particular) comprising forming a suspension of **autologous epidermal cells** and a soluble medium (and that can further comprise growth factor such as fetal calf serum; antibiotics such as penicillin and streptomycin; see pages 1210-1211, right column, in particular); placing the cell suspension into a receptacle (see figure 1 for the device and parts, page 1208, in particular) of an air-jet sprayer (a commercial aerosolization device that uses compressed air, as shown in figure 1; having a nozzle orifice with a pore size sufficient to allow passage of cells without damaging dispensed cells); and dispersing the cells through the nozzle orifice onto an area of skin of a subject lacking normal, healthy skin (using pigs as experimental animals with full-thickness wounds on the back taken as area of skin lacking normal, healthy skin; see pages 1210-1211, in particular) using the air-jet sprayer; wherein the method further comprises growing a three-dimensional epithelial tissue from the cells in the area lacking normal, healthy skin (see table II-III, figures 3 and 5, and page 1212, in particular). In addition, it is to be noted that Cohen et al explicitly suggest an alternative method such as "to use the cells (i.e. subject's autologous epidermal cells that also contain stem cells) along with a dermal graft or dermal substitute" (see Cohen et al, page 1214, left column, 1st paragraph, in

particular), and thus invite such modification and/or combination in the method of dispersing living cells onto an area of skin (even with unfavorable topography) of a subject lacking normal, healthy skin using an air-jet spray device, as recited by the instant invention.

However, a method according to claim 11, wherein the **suspension consists of autologous stem cells** and a soluble medium, is not explicitly exemplified by the referenced invention of Marshall et al, or Cohen et al.

Sorrell et al [A2] disclose the isolation, in vitro culture and expansion, and therapeutic use of **mesenchymal stem cells** (MSCs) in forming multilayer skin or dermal equivalent (see abstract, summary of the invention, column 8 and 9, in particular), wherein suspension of autologous human MSCs are used in various tissue regeneration procedures including burn and wound/laceration management.

Therefore, given the fact that Marshall et al or Cohen et al explicitly disclose a method for aerosolized or spray delivery of living cells (using a suitable device such as an air-jet sprayer), including keratinocytes or epidermal cell suspensions (which are known in the art to contain stem cells) with or without fibrin sealant onto a target area such as skin wound, and further disclose spray delivery for fibroblasts (see column 2, 2nd paragraph, and column 3, 1st paragraph, in particular) and other suitable cells, it would have been obvious to a person of ordinary skill in the tissue-repair or regeneration art (at the time the claimed invention was made) to modify the method of Marshall et al or Cohen et al such that the method comprises the step of forming a suspension consisting of a subject's autologous stem cells (i.e. substituting a better functional equivalent; for their potential for enhancing tissue repair and regeneration

which is well documented in the wound healing prior art) and a soluble medium, which is clearly suggested by the disclosure of Sorrell et al [A] for forming a dermal equivalent.

The specific limitation of separately delivering at least one different type of autologous cell suspension would have been a matter of routine arrangement and optimization of the method steps to an artisan of ordinary skill in the art, as evidenced by the fact that Marshall et al disclose individual delivery of autologous keratinocytes, and co-delivery of keratinocytes and fibroblasts (see column 5, 3rd paragraph, column 6, lines 41-46, in particular), and further suggest the fact that the device can be modified to provide more outlets, etc. (see column 8, 1st paragraph, in particular) depending on the need. In absence of any criticality attached (or demonstrated by applicants in the original disclosure as filed with the office) for the method step of "forming a suspension consisting of a subject's autologous stem cells and a soluble medium" that is dispersed onto the skin of the desired subject in need thereof, such method steps of using or dispersing autologous stem cells, alone or in combination with at least one other type of autologous cell suspension, would have been obvious to an artisan of ordinary skill in the tissue regeneration art when taking the combined disclosures of cited prior art into consideration, and accordingly would have had a reasonable expectation of success in modifying the method of dispersing living cells, as discussed above.

Thus, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the art at the time the claimed invention was made.

> As per MPEP 2144.04, *Ex parte Rubin, 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the* ***order of the prior art process steps****.). See also In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA*

1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

As per MPEP 2111.01, during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004)(The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

Response to Applicant's Arguments

Applicant's arguments filed with the office on March 6th 2008 (as they pertain to the obviousness rejection of record) have been fully considered but they are moot in view of the new ground of rejection made in this office action.

Pertinent Prior Art Not Relied Upon in Rejections

1. **ROLLAND et al (US Patent 7,144,729 B2; filed on Dec. 19, 2002),** Methods and compositions for tissue regeneration (discloses a method of dispersing isolated, living cell suspensions containing keratinocytes and fibroblast cells, or a mixture thereof onto a wound site using a suitable spray applicator, with or without fibrin glue, with or without scaffold, or dermal allografts, wherein the order of spraying the components can be readily modified or rearranged depending on the need; see abstract, summary of the invention, figures 4-6, column 7, 21-22, 25-26, and examples such as examples 16-17, in particular).

2. **GRANT I. et al.** The co-application of sprayed cultured autologous keratinocytes and autologous fibrin sealant in a porcine wound model, British J. of Plastic Surgery, 2002, 55: 219-227 (see summary, materials and methods, in particular).

3. **NAVARRO F.A. et al**. Sprayed keratinocytes suspensions accelerate epidermal coverage in a porcine microwound model, J. Burn Care Rehabil., 2000, 21: 513-518 (see abstract and introduction on page 513, Material and Methods, figure 1, and cited reference 8, in particular).

4. **NAVARRO F.A. et al.** Melanocyte repopulation in full-thickness wounds using a cell spray apparatus, J. Burn Care Rehabil., 2001, 22: 41-46 (see abstract on page 41, and materials & methods, in particular).

Conclusion

NO claims are allowed.

Applicants are advised that the prior art rejection under 35 USC 102(b) over COHEN et al [U] has been **withdrawn in view of the current claim amendments** that are deemed to constitute "**new matter**" as discussed above (see 35 USC 112, first paragraph rejection *supra*), and may be relied upon or re-instated in future depending upon further claim amendments during prosecution.

Furthermore, applicants should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP § 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 USC §102 or 35 USC §103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to the office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SATYENDRA K. SINGH whose telephone number is (571)272-8790. The examiner can normally be reached on 9-5MF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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